

### Claims

1. A method for the detection, differentiation and prognosis of a gynaecological cell proliferative disorder comprising the following steps:
  - a) obtaining a cervicovaginal secretion specimen from an individual
  - b) determining the methylation status of at least one or more CpG positions
  - c) determining from said methylation status the presence, classification and/or prognosis of a gynaecological cell proliferative disorder in said individual.
2. The method according to claim 1 wherein said CpG positions are selected from one or more genes taken from the group consisting of SFRP2, SFRP4, SFRP5, CCND2, CDH1, CDH13, RASSF1A, hMLH1, HSPA2, SOCS1, SOCS2, GSTP1, DAPK, TIMP3 and hTERT.
3. The method according to claim 1 wherein said CpG positions are selected from one or more sequences taken from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 11 and SEQ ID NO: 64 to SEQ ID NO: 67.
4. A method according to claim 1 wherein in step a) the specimen is obtained by one or more of the following methods gynaecological swab, aspiration, cervicovaginal lavage and tampon based collection.
5. The method according to claims 1 and 2 wherein the gynaecological cell proliferative disorder is selected from the group consisting no dysplasia or low grade squamous intraepithelial lesions, high-grade squamous intraepithelial lesions, cervical cancer, endometrial cancer and grade 1 to 3 cervical intraepithelial neoplasia.
6. The method according to claim 1 wherein hypermethylation of said genes correlates with bad prognosis.
7. The method according to claim 1 wherein step b) comprises the following steps

- a) treating the genomic DNA, or a fragment thereof, with one or more reagents to convert 5-position unmethylated cytosine bases to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties;
  - b) contacting the treated genomic DNA, or the treated fragment thereof, with an amplification enzyme and at least two primers comprising, in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a target nucleic acid, and
  - c) determining, based on a presence or absence of, or on a property of said amplificate, the methylation state of at least one CpG dinucleotide sequence, or an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotide sequences, whereby at least one of detecting a gynecological cell proliferative disorder, or distinguishing between gynecological cell proliferative disorders is, or providing a prognosis at least in part, afforded.
8. The method according to claim 7 wherein in step b) the target nucleic acid is selected from the group consisting of SEQ ID NO: 12 to SEQ ID NO: 55 and SEQ ID NO: 68 to SEQ ID NO: 83.
  9. A nucleic acid molecule or peptide nucleic acid molecule comprising, in each case a contiguous sequence of at least 9 nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 55 and SEQ ID NO: 64 to SEQ ID NO: 83, and complements thereof.
  10. A nucleic acid according to claim 9, wherein the sequence is selected from the group consisting of SEQ ID NO: 12 to SEQ ID NO: 55 and SEQ ID NO: 68 to 83.
  11. A nucleic acid according to claim 10, wherein the nucleic acid molecule comprises at least one TpA or CpA dinucleotide at a position where the corresponding untreated nucleic acid molecule according to SEQ ID NO: 1 to SEQ ID NO: 11 and SEQ ID NO: 64 to SEQ IDNO: 67 comprises a CpG dinucleotide.
  12. A kit useful for detecting, or for detecting distinguishing between or among gynecological cell proliferative disorders of a subject, comprising:

at least one of a bisulfite reagent, or a methylation-sensitive restriction enzyme; and at least one nucleic acid molecule or peptide nucleic acid molecule comprising, in each case a contiguous sequence of at least 9 nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID: 12 to SEQ ID NO: 55 and SEQ ID NO: 68 to SEQ ID NO: 83, and complements thereof.

13. The kit of claim 12, further comprising standard reagents for performing a methylation assay selected from the group consisting of MSP, MethyLight and HeavyMethyl and combinations thereof.